

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oramox (Amoxicillin Oral Suspension BP) 250mg/5ml.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of reconstituted suspension contains Amoxicillin Trihydrate, equivalent to 250 mg of Amoxicillin.

Excipients: Each 5ml contains 2700 mg of sucrose and 6.47mg of sodium.

For the full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Powder for oral suspension

A pale yellow crystalline powder for oral suspension with the odour and flavour of lemon

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of infections due to organisms sensitive to Amoxicillin and in the oral prophylaxis of endocarditis related to dental procedures, and acute uncomplicated gonorrhoea and dental abscess (as an adjunct to surgical management).

4.2 Posology and method of administration

Oramox Suspensions are for oral use.

The absorption of Oramox is virtually unimpaired by the presence of food.

Adults and children weighing over 40kg

Standard adult dosage: The usual daily dosage is 750mg in divided doses (i.e. 250mg three times daily by the oral route). In cases of severe infection the dosage may be doubled, or amoxicillin given by injection.

High dosage therapy: (maximum recommended oral dosage of 6g daily in divided doses): A dosage of 3g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Short course therapy:

Simple acute urinary tract infection: two 3g doses with 10-12 hours between the doses.

Gonorrhoea: 3g as a single dose.

Dental Abscess: two 3g doses with 8 hours between the doses.

Prophylaxis of endocarditis

For dental procedures where an oral dose is appropriate:

Adults and children weighing over 40kg: 3g dose followed by (6 hours later) a further 3g dose (or a 1g IM if oral dose not tolerated) if necessary.

Paediatric population

Children weighing < 40 kg

The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses* (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen (see special dosage recommendations

below and sections 4.4, 5.1 and 5.2).

*PK/PD data indicate that dosing three times daily is associated with enhanced efficacy, thus twice daily dosing is only recommended when the dose is in the upper range.

Children weighing more than 40 kg should be given the usual adult dosage.

Special dosage recommendation

Tonsillitis: 50 mg/kg/day in two divided doses.

Acute otitis media: In areas with high prevalence of pneumococci with reduced susceptibility to penicillins, dosage regimens should be guided by national/local recommendations.

Early Lyme disease (isolated erythema migrans): 50 mg/kg/day in three divided doses, over 14-21 days.

Prophylaxis for endocarditis

Paediatric population:

50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure.

Dosage in impaired renal function

The dose should be reduced in patients with severe renal function impairment. In patients with a creatinine clearance of less than 30 ml/min an increase in the dosage interval and a reduction in the total daily dose is recommended (see section 4.4 and 5.2).

Renal impairment in adults and children weighing over 40kg:

Glomerular filtration rate	Oral treatment
> 30 ml/min	No adjustment necessary
10-30 ml/min	Oramox Max 500mg b.d.
< 10ml/min	Oramox Max 500mg/day

Renal impairment in children under 40 kg:

Creatinine clearance ml/min	Dose	Interval between administration
> 30	Usual dose	No adjustment necessary
10 – 30	Usual dose	12 h (corresponding to 2/3 of the dose)
< 10	Usual dose	24 h (corresponding to 1/3 of the dose)

For small children (younger than 6 years of age) appropriate paediatric formulation should be used.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Use in patients with a history of hypersensitivity to beta-lactam antibiotics including penicillins, ampicillins or to cephalosporins.

4.4 Special warnings and precautions for use

Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients receiving beta-lactam antibiotics. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in persons with a history of penicillin hypersensitivity and/or a

history of sensitivity to multiple allergens. Attention should also be paid to possible cross-reactivity with other beta-lactam antibiotics e.g. cephalosporins (see section 4.3)

If an allergic reaction occurs, amoxicillin should be discontinued and appropriate therapy should be instituted

Amoxicillin should be avoided if infectious mononucleosis (glandular fever) is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Prolonged use of anti-infective agent may result in super infection by organisms resistant to that anti-infective.

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Dosage should be adjusted in patients with renal impairment (see Section 4.2).

In patients with reduced urine output crystalluria has been observed very rarely predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria.

In patients with renal impairment, the rate of excretion of amoxicillin will be reduced depending on the degree of impairment and it may be necessary to reduce the total daily unit amoxicillin dosage accordingly.

Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.

Precaution should be taken in premature children and during the neonatal period: renal, hepatic and haematological functions should be monitored.

Oramox Oral Suspension BP 250mg/5ml contains 3.054g of sucrose per 5ml dose. This should be taken into account in patients with diabetes mellitus.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicinal product contains 6.46mg of sodium per 5ml dose. To be taken into consideration by patients on controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

When administered concurrently, the following drugs may interact with amoxicillin:

Bacteriostatic antibiotics

Chloramphenicol, erythromycins, sulfonamides or tetracyclines may interfere with the bactericidal effects of penicillins. This has been demonstrated in vitro; however, the clinical significance of this interaction is not well documented.

Probenecid

Probenecid may decrease renal tubular excretion of amoxicillin resulting in increased blood levels and/or amoxicillin toxicity.

Drug/Laboratory Test Interactions

After treatment with amoxicillin, a false-positive reaction for glucose in the urine may occur with copper sulphate tests (Benedict's solution, Fehling's solution, or Clinitest tablets) but not with enzyme based tests such as Clinistix and Test-Tape.

Allopurinol

Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Methotrexate

Interaction between amoxicillin and methotrexate leading to methotrexate toxicity has been reported. Serum methotrexate levels should be closely monitored in patients who receive amoxicillin and methotrexate simultaneously. Amoxicillin decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system.

Anticoagulants

In the literature there are rare cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies with 'Oramox' have shown no teratogenic effects. The product has been in extensive clinical use since 1972 and its suitability to human pregnancy has been well documented in clinical studies. Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with the treatment.

Breast-feeding

Amoxicillin may be administered during the period of lactation.

With the exception of the risk of sensitisation and of central nervous system toxicity (due to prematurity of the blood-brain barrier) associated with the excretion of trace quantities of amoxicillin in breast milk, there are no known detrimental effects for the infant.

4.7 Effects on ability to drive and use machines

Amoxicillin has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Evaluation of undesirable effects is based on the following frequency information: very common (> 1/10); common ($\geq 1/100$ to <1/10); uncommon ($\geq 1/1,000$ to <1/100); rare ($\geq 1/10,000$ to <1/1,000); very rare (<1/10,000); not known (frequency cannot be estimated from available data).

The majority of side effects listed below are not unique to amoxicillin and may occur when using other penicillins.

Unless otherwise stated, the frequency of adverse events (AEs) has been derived from more than 30 years of post-marketing reports.

Blood and lymphatic system disorders:

Very rare: Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia.

Prolongation of bleeding time and prothrombin time (*refer to section 4.4*)

Immune System disorders:

Very rare: As with other antibiotics, severe allergic reactions including angioneurotic oedema and anaphylaxis (See section 4.4). Serum sickness like syndrome and hypersensitivity vasculitis.

If hypersensitivity reaction occurs, the treatment must be discontinued. (See also Skin and subcutaneous tissue disorders)

Nervous system disorders:

Very rare: Hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses. Aseptic meningitis.

Infections and Infestations:

Very rare: Mucocutaneous candidiasis

Gastrointestinal disorders:

*Common: Diarrhoea and nausea

*Uncommon: Vomiting,

Very rare: Antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis)
Black hairy tongue

Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing (for suspension and chewable tablet formulations only).

Hepato-biliary disorders:

Very rare: Hepatitis and cholestatic jaundice. A moderate rise in AST or ALT. The significance of a rise in AST and/or ALT is unclear.

Skin and subcutaneous tissue disorders:

*Common: Skin rash,

*Uncommon: Pruritus and urticaria.

Very rare: Skin reactions such as erythema multiforme and Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP), (See also Immune System Disorders)

Renal and Urinary Tract disorders:

Very rare: Interstitial nephritis, crystalluria (see Section 4.9 Overdose).

*The incidence of these AEs was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

HPRA Pharmacovigilance
Earlsfort Terrace
IRL- Dublin 2
Tel: + 353 1 6764971
Fax: + 353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

4.9 Overdose

Gross overdose will produce very high urinary concentration, more so after parenteral administration. Symptoms of water/electrolyte imbalance should be treated symptomatically. Problems are unlikely to occur if adequate fluid intake and urinary output are maintained; however amoxicillin crystalluria in some cases leading to renal failure, has been observed (see Section 4.4, Special Warnings and Precautions for use). More specific measures may be required in

patients with impaired renal function: the antibiotic is removed by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amoxicillin is semisynthetic penicillin, which is acid resistant and has a similar antibacterial spectrum to Ampicillin. It acts by inhibiting bacterial cell-wall synthesis.

It is, however, better absorbed after oral administration, yielding blood levels approximately twice as high as those obtained with similar doses of Ampicillin.

Amoxicillin is used for the same purposes as Ampicillin and is especially suitable for the treatment of infections of the urinary and respiratory tracts by Ampicillin sensitive organisms.

5.2 Pharmacokinetic properties

Absorption:

Amoxicillin is stable to gastric acid and 50 - 90% of a dose is absorbed after oral administration: absorption is more complete than that of Ampicillin and it is not greatly influenced by the presence of food.

Blood Concentration:

After an oral dose of 500mg, peak serum concentration of 3 to 20ug/ml are attained in 1 to 2 hour, detectable concentrations are present after 8 hours. Peak concentrations occur earlier in children and infants, but later in neonates.

Half-life:

Serum half-life, 1 hour which may be increased to 15 hours in renal failure.

Distribution:

Enters most tissues and fluid but is not detectable in the cerebrospinal fluid even when meninges are inflamed; crosses the placenta and small amounts are secreted in the milk; volume of distribution at steady-state serum concentrations, about 0.3 litres/kilogram body weight; protein binding, 15 - 25% bound to plasma protein.

Metabolic Reactions:

Metabolised to inactive metabolites and 10 - 25% appears to be converted to penicilloic acid.

Excretion:

35 - 45% is excreted in the urine after an oral dose; urinary excretion is delayed by probenecid and it also occurs more slowly in the newborn; small amounts are excreted in the bile

In preterm infants with gestational age 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75-2 ml/min, very similar to the inulin clearance (GFR) in this population. Following oral administration, the absorption pattern and the bioavailability of amoxicillin in small children may be different to that of adults. Consequently, due to the decreased CL, the exposure is expected to be elevated in this group of patients, although this increase in exposure may in part be diminished by decreased bioavailability when given orally.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Benzoate (E211)
Disodium Edetate
Sodium Citrate Anhydrous
Lemon Flavour Powder
Quinoline Yellow (E104)
Sucrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

As packaged for sale: 2 years

After reconstitution: 7 days

6.4 Special precautions for storage

Powder:- Do not store above 25°C. Store in the original package. Keep the bottle tightly closed.

Reconstituted suspension:- After mixing, the suspension should be stored at 2°C - 8°C in a refrigerator

6.5 Nature and contents of container

Natural high-density polyethylene bottle with a tamper evident cap packed in an outer carton.

A spoon with graduations of 1.25ml, 2.5ml and 5ml or a spoon with just 5ml graduation may be supplied with this pack of this product.

Pack size: 100ml.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

To prepare a 100 ml suspension add 61 mls of water and shake well.

After reconstitution, the product appears as a yellow suspension with the odour and flavour of lemon.

7 MARKETING AUTHORISATION HOLDER

Athlone Laboratories Limited
Ballymurray
Co. Roscommon

8 MARKETING AUTHORISATION NUMBER

PA0298/019/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 September 1988

Date of last renewal: 27 September 2008

10 DATE OF REVISION OF THE TEXT

24 February 2016